UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/553,993 | 04/20/2000 | Kevin Gunderson | A-69235/DJB/RMS/DCF | 5906 |

7590 05/14/2004

Pillsbury Winthrop LLP
Intellectual Property Group
11682 El Camino Real
Suite 200
San Diego, CA 92130

| EXAMINER | |
|---|---|
| FORMAN, BETTY J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/553,993 | GUNDERSON ET AL. | |
| | Examiner | Art Unit | |
| | BJ Forman | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *15-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *0504*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2 March 2004 has been entered.

### *Status of the Claims*

2. This action is in response to papers filed 2 March 2004 in which claims 15-22, 24 and 27-29 were amended. All of the amendments have been thoroughly reviewed and entered.

The previous objections and rejections in the Office Action dated 2 October 2003, not reiterated below, are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 103 are maintained in view of the new matter rejection below.

Applicant's arguments have been thoroughly reviewed. Applicant states that none of the cited references teach or suggest the instant claims. The arguments have been considered but are not found persuasive for the reasons stated below. New grounds for rejection are discussed.

Claims 15-29 are under prosecution.

***Claim Rejections - 35 USC § 112***

**35 U.S.C. 112: First paragraph**

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 15-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent Claims 22 and 29 (from which all pending claims depend) have been amended to define the target sequence as immobilized on a solid phase. Applicant points to page 69, lines 22-26 and the last paragraph of page 79 for support of the amendments. The passages have been reviewed. The paragraph beginning at line 22 of page 69 describes an immobilized target and references the embodiment illustrated in Fig. 10. Figure 10 illustrates the target immobilized via hybridization to an immobilized capture probe attached to the microsphere on a solid support. While the specification provides support for the newly claimed immobilized target, the immobilized target taught by the specification encompasses immobilization via hybridization to capture probes as illustrated in the instant specification. However, the specification does not teach or describe the instantly claimed methods of

hybridizing an immobilized target with a primer having an adapter sequence and subsequently contacting the adapter sequence with an array of microspheres comprising a capture probe. Hence, the claims as amended, introduce new matter into the specification.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

**35 U.S.C. 112: Second paragraph**

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 15-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29 and 15-21 are indefinite in Claim 29, step f for the recitation "said nucleic acid sequence" because the recitation lacks proper antecedent basis in the "target nucleic acid sequence" in the preamble. The recitation is further indefinite because it is unclear whether detection of the nucleic acid detects the target nucleic acid as claimed.

Claims 22-28 are indefinite in Claim 22 because the claim is drawn to "simultaneously detecting at least sixteen target nucleic acid sequences". However, the method steps do not

detect a target nucleic acid sequence, do not detect sixteen target nucleic acid sequences and do not simultaneously detect at least sixteen target nucleic acid sequences. Therefore, it is unclear whether the method steps accomplish the claimed method.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**Maintained from the previous rejection in view of the New Matter Rejection**

8. Claims 29, 15-17, 19-20, 22-24 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz (U.S. Patent No. 6,280,935, filed 4 June 1998) in view of Ullman et al (U.S. Patent No. 5,185,243, issued 9 February 1993).

Regarding Claim 29, Macevicz teaches a method of detecting a target nucleic acid sequence, said method comprising: hybridizing a first primer portion comprising an adapter sequence (ligation probe) to a target sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primer to form a modified primer; contacting said modified primer with an array comprising: a substrate with a surface comprising discrete sites and a population of microspheres comprising a first nucleic acid capture probe that hybridizes to said adapter sequence wherein said microspheres are

distributed on said surface and detecting the presence of said target sequence (Column 34, lines 11-38). Macevicz does not teach that the first and second portions of the target sequences are non adjacent and extending either the first or second primer toward the other.

However, Ullman et al teach a similar method comprising: hybridizing a first primer portion to a target sequence; hybridizing a second primer to a second portion of said target sequence wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Macevicz by designing primers that hybridize to non-adjacent target positions as taught by Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Regarding Claim 15, Macevicz teaches the method further comprising detecting a second target sequence (i.e. population of library members) thereby comprising hybridizing third and forth primers to first and second portions of the second target; contacting with said array and detecting the presence of said second target (Column 16, lines 12-67).

Regarding Claim 16, Macevicz teaches the method wherein the modified primer is amplified (Column 16, line10-Column 19, line 49).

Regarding Claim 17, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

Regarding Claim 19, Macevicz discloses the method wherein said discrete sites comprise wells (Column 32, lines 5-10).

Regarding Claim 20, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

Regarding Claim 22, Macevicz teaches a method of detecting a plurality of target nucleic acid sequences, (i.e. population of library members, Column 16, lines 12-67) said method comprising: hybridizing a first primer portion comprising an adapter sequence (ligation probe) to a target sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primer to form a modified primer; contacting said modified primer with an array comprising: a substrate with a surface comprising discrete sites and a population of microspheres comprising a first nucleic acid capture probe that hybridizes to said adapter sequence wherein said microspheres are distributed on said surface and detecting the presence of said target sequence (Column 34, lines 11-38). Macevicz does not teach that the first and second portions of the target sequences are non adjacent and extending either the first or second primer toward the other.

However, Ullman et al teach a similar method comprising: hybridizing a first primer portion to a target sequence; hybridizing a second primer to a second portion of said target sequence wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Macevicz by designing primers that hybridize to

non-adjacent target positions as taught by Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Regarding Claim 23, Macevicz teaches the method wherein the modified primer is amplified (Column 16, line10-Column 19, line 49).

Regarding Claim 24, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

Regarding Claim 26, Macevicz discloses the method wherein said discrete sites comprise wells (Column 32, lines 5-10).

Regarding Claim 27, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

**Maintained from the previous rejection in view of the New Matter Rejection**

9. Claims 18 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz (U.S. Patent No. 6,280,935, filed 4 June 1998) in view of Ullman et al (U.S. Patent No. 5,185,243, issued 9 February 1993) as applied to Claims 29 and 22 above and further in view of Walt et al (U.S. Patent No. 6327,410, filed 11 September 1998).

Regarding Claims 18 and 25, Macevicz teaches a method of detecting a target nucleic acid sequence and a library of targets, said method comprising: hybridizing a first primer portion comprising an adapter sequence (ligation probe) to a target sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primer

to form a modified primer; contacting said modified primer with an array comprising: a substrate with a surface comprising discrete sites and a population of microspheres comprising a first nucleic acid capture probe that hybridizes to said adapter sequence wherein said microspheres are distributed on said surface and detecting the presence of said target sequence (Column 34, lines 11-38). And Ullman et al teach a similar method comprising: wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12).

Macevicz further teaches the substrate is selected from one of many known in the art and is selected based on efficiency and optical properties (Column 14, line 61-Column 15, line 23, especially lines 17-21) but they do not specifically teach the support is a fiber optic bundle. However, Walt et al teach a similar method of target detection comprising contacting a modified target sequence with an array comprising a substrate with a patterned surface comprising discrete sites and a population of microspheres comprising a first and second subpopulation capture probe wherein the microspheres are distributed on said patterned surface and detecting the presence of said first modified target sequence wherein said target is labeled prior to contacting (Column 21, lines 17-25) wherein they specifically teach that their fiber optic bundle support, in addition to providing optical properties which permit optical resolution of tens of thousands of target sequences, is efficient and inexpensive (Column 4, lines 35-58 and Column 5, lines 24-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the fiber optic support of Walt et al to the support of Macevicz based on the suggestion of Macevicz to apply known supports based on efficiency and optical properties (Column 14, line 61-Column 15, line 23, especially lines 17-

21) and for the expected benefits of exceptional efficiency and optical properties as taught by Walt et al (Column 4, lines 35-58 and Column 5, lines 24-30).

**Maintained from the previous rejection in view of the New Matter Rejection**

10. Claims 15-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. (U.S. Patent No. 6,027,889, filed 28 May 1997) in view of Ullman et al (U.S. Patent No. 5,185,243, issued 9 February 1993) and Walt et al. (U.S. Patent No. 6,023,540, filed 14 may 1997).

Regarding Claim 29, Barany et al. teach a method of detecting a target nucleic acid sequence comprising: hybridizing a first primer to a first portion of a target sequence wherein said first primer further comprises an adapter sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primers to form a modified primer; contacting said adapter sequence of said modified primer with an array comprising: a substrate with a surface comprising discrete sites comprising at least a first sub-population comprising a first capture probe, such that said first capture probe and said modified first target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified first target nucleic acid sequence (Column 26, line 37-Column 27, line 19 and Claim 13). The extra method steps of Barany et al. are encompassed by the open claim language "comprising" of the instant claims.

Barany et al. do not teach the method wherein the primers are not adjacent. However, Ullman et al teach a similar method comprising: wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-

Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Barany et al by designing primers that hybridize to non-adjacent target positions as taught by Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Barany et al. do not teach the method wherein the array further comprises a population of microspheres comprising the at least first sub-population wherein said microspheres are distributed on said surface. However, Walt et al. teach a similar method for detecting a target nucleic acid sequence comprising: contacting said first target nucleic acid sequence with an array comprising: a substrate with a patterned surface comprising discrete sites; and a population of microspheres comprising at least a first sub-population comprising a first capture probe such that said first capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said first target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual

identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 15, Barany et al. teach the method further comprising detecting a second target sequence (i.e. array) thereby comprising hybridizing third and forth primers to first and second portions of the second target; contacting with said array and detecting the presence of said second target (Fig. 9).

Regarding Claim 16, Barany et al. teach the method wherein the modified primer is amplified (Column 27, lines 1-2).

Regarding Claim 17, Barany et al. teach the method wherein said the detecting is done by hybridizing a labeled probe to the ligated primers (Column 33, lines 16-39).

Regarding Claim 18, Barany et al. teach the substrate is an array (Column 27, lines 10-15) but they do not teach the array is a fiber optic bundle. However, Walt et al. teach the similar method wherein the substrate is a fiber optic bundle (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on a fiber optic bindle substrate for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 19, Barany et al. teach said substrate comprises discrete sites (Column 27, lines 10-15) but they do not teach said discrete sites comprise wells. However, Walt et al. teach the similar method wherein said discrete sites comprise wells (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the discrete sites on the substrate of Barany et al. to provide microspheres distributed on a substrate at the discrete sites and wherein each discrete site comprises a well for the expected benefit of individual identification of thousands of captured

target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 20, Barany et al teach the method wherein the detecting is done by labeling amplification products (Column 27, liens 2-19).

Regarding Claim 21, Barany et al teach the method wherein one of the primers is allele specific (Column 25, lines 1-25).

Regarding Claim 22, Barany et al. teach a method of detecting at least sixteen target nucleic acids (i.e. an array, Fig. 9) sequence comprising: hybridizing a first primer to a first portion of a target sequence wherein said first primer further comprises an adapter sequence; hybridizing a second primer to a second portion of said target sequence;ligating said first and second primers to form a modified primer; contacting said adapter sequence of said modified primer with an array comprising: a substrate with a surface comprising discrete sites comprising at least a first sub-population comprising a first capture probe, such that said first capture probe and said modified first target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified first target nucleic acid sequence (Fig. 15, Column 26, line 37-Column 27, line 19 and Claim 13). The extra method steps of Barany et al. are encompassed by the open claim language "comprising" of the instant claims.

Barany et al. do not teach the method wherein the primers are extended toward each other. However, Ullman et al teach a similar method comprising: extending one primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Barany et al by designing primers that hybridize to non-adjacent target positions as taught by

Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Barany et al. do not teach the method wherein the array further comprises a population of microspheres comprising the at least first sub-population wherein said microspheres are distributed on said surface. However, Walt et al. teach a similar method for detecting a target nucleic acid sequence comprising: contacting said first target nucleic acid sequence with an array comprising: a substrate with a patterned surface comprising discrete sites; and a population of microspheres comprising at least a first sub-population comprising a first capture probe such that said first capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said first target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 23, Barany et al. teach the method wherein the modified primer is amplified (Column 27, lines 1-2).

Regarding Claim 24, Barany et al. teach the method wherein said the detecting is done by hybridizing a labeled probe to the ligated primers (Column 33, lines 16-39).

Regarding Claim 25, Barany et al. teach the substrate is an array (Column 27, lines 10-15) but they do not teach the array is a fiber optic bundle. However, Walt et al. teach the similar method wherein the substrate is a fiber optic bundle (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on a fiber optic bindle substrate for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 26, Barany et al. teach said substrate comprises discrete sites (Column 27, lines 10-15) but they do not teach said discrete sites comprise wells. However, Walt et al. teach the similar method wherein said discrete sites comprise wells (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the discrete sites on the substrate of Barany et al. to provide microspheres distributed on a substrate at the discrete sites and wherein each discrete site comprises a well for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 27, Barany et al teach the method wherein the detecting is done by labeling amplification products (Column 27, liens 2-19).

Regarding Claim 28, Barany et al teach the method wherein one of the primers is allele specific (Column 25, lines 1-25).

**New grounds for rejection**

11. Claims 29, 15-17, 19-20, 22-24 and 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz (U.S. Patent No. 6,280,935, filed 4 June 1998) in view of Ullman et al (U.S. Patent No. 5,185,243, issued 9 February 1993) and Collins (U.S. Patent No. 5,750,338, issued 12 May 1998).

Regarding Claim 29, Macevicz teaches a method of detecting a target nucleic acid sequence, said method comprising: hybridizing a first primer portion comprising an adapter sequence (ligation probe) to a target sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primer to form a modified primer; contacting said modified primer with an array comprising: a substrate with a surface comprising discrete sites and a population of microspheres comprising a first nucleic acid capture probe that hybridizes to said adapter sequence wherein said microspheres are distributed on said surface and detecting the presence of said target sequence (Column 34, lines 11-38). Macevicz does not teach that the first and second portions of the target sequences are non adjacent and extending either the first or second primer toward the other.

However, Ullman et al teach a similar method comprising: hybridizing a first primer portion to a target sequence; hybridizing a second primer to a second portion of said target sequence wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Macevicz by designing primers that hybridize to

non-adjacent target positions as taught by Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Macevicz and Ullman do not teach the target is immobilized on a solid phase surface during hybridization between the first primer and target. However, target immobilization during a first hybridization step was well known in the art at the time the claimed invention was made as taught by Collins (e.g. Fig.6). Collins et al teach a similar method of target detection comprising a first step of hybridizing a first primer and a target, wherein the target is immobilized whereby the target immobilization facilitates removal of non-specific material from the sample and concentrates the target for detection and greater purification of detectable product (Column 5, lines 19-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the target immobilization of Collins et al to the target detection of Macevicz and Ullman for the expected benefit removal of non-specific material from the sample, concentration the target for detection and greater purification of detectable product as taught by Collins (Column 5, lines 19-25).

Regarding Claim 15, Macevicz teaches the method further comprising detecting a second target sequence (i.e. population of library members) thereby comprising hybridizing third and forth primers to first and second portions of the second target; contacting with said array and detecting the presence of said second target (Column 16, lines 12-67).

Regarding Claim 16, Macevicz teaches the method wherein the modified primer is amplified (Column 16, line10-Column 19, line 49).

Regarding Claim 17, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

Regarding Claim 19, Macevicz discloses the method wherein said discrete sites comprise wells (Column 32, lines 5-10).

Regarding Claim 20, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

Regarding Claim 22, Macevicz teaches a method of detecting a plurality of target nucleic acid sequences, (i.e. population of library members, Column 16, lines 12-67) said method comprising: hybridizing a first primer portion comprising an adapter sequence (ligation probe) to a target sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primer to form a modified primer; contacting said modified primer with an array comprising: a substrate with a surface comprising discrete sites and a population of microspheres comprising a first nucleic acid capture probe that hybridizes to said adapter sequence wherein said microspheres are distributed on said surface and detecting the presence of said target sequence (Column 34, lines 11-38). Macevicz does not teach that the first and second portions of the target sequences are non adjacent and extending either the first or second primer toward the other.

However, Ullman et al teach a similar method comprising: hybridizing a first primer portion to a target sequence; hybridizing a second primer to a second portion of said target sequence wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Macevicz by designing primers that hybridize to

non-adjacent target positions as taught by Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Macevicz and Ullman do not teach the target is immobilized on a solid phase surface during hybridization between the first primer and target. However, target immobilization during a first hybridization step was well known in the art at the time the claimed invention was made as taught by Collins (e.g. Fig.6). Collins et al teach a similar method of target detection comprising a first step of hybridizing a first primer and a target, wherein the target is immobilized whereby the target immobilization facilitates removal of non-specific material from the sample and concentrates the target for detection and greater purification of detectable product (Column 5, lines 19-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the target immobilization of Collins et al to the target detection of Macevicz and Ullman for the expected benefit removal of non-specific material from the sample, concentration the target for detection and greater purification of detectable product as taught by Collins (Column 5, lines 19-25).

Regarding Claim 23, Macevicz teaches the method wherein the modified primer is amplified (Column 16, line10-Column 19, line 49).

Regarding Claim 24, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

Regarding Claim 26, Macevicz discloses the method wherein said discrete sites comprise wells (Column 32, lines 5-10).

Regarding Claim 27, Macevicz discloses the method wherein the detecting is done by hybridizing a labeled probe (Column 24, lines 63-67). And Ullman et al teach their similar method wherein the detecting is done by hybridizing a labeled probe (Column 22, lines 9-42).

12. Claims 18 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macevicz (U.S. Patent No. 6,280,935, filed 4 June 1998) in view of Ullman et al (U.S. Patent No. 5,185,243, issued 9 February 1993) and Collins (U.S. Patent No. 5,750,338, issued 12 May 1998) as applied to Claims 29 and 22 above and further in view of Walt et al (U.S. Patent No. 6327,410, filed 11 September 1998).

Regarding Claims 18 and 25, Macevicz teaches a method of detecting a target nucleic acid sequence and a library of targets, said method comprising: hybridizing a first primer portion comprising an adapter sequence (ligation probe) to a target sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primer to form a modified primer; contacting said modified primer with an array comprising: a substrate with a surface comprising discrete sites and a population of microspheres comprising a first nucleic acid capture probe that hybridizes to said adapter sequence wherein said microspheres are distributed on said surface and detecting the presence of said target sequence (Column 34, lines 11-38). And Ullman et al teach a similar method comprising: wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12).

Macevicz further teaches the substrate is selected from one of many known in the art and is selected based on efficiency and optical properties (Column 14, line 61-Column 15, line 23, especially lines 17-21) but they do not specifically teach the support is a fiber optic bundle. However, Walt et al teach a similar method of target detection comprising contacting a modified target sequence with an array comprising a substrate with a patterned surface comprising discrete sites and a population of microspheres comprising a first and second subpopulation capture probe wherein the microspheres are distributed on said patterned surface and detecting the presence of said first modified target sequence wherein said target is labeled prior to contacting (Column 21, lines 17-25) wherein they specifically teach that their fiber optic bundle support, in addition to providing optical properties which permit optical resolution of tens of thousands of target sequences, is efficient and inexpensive (Column 4, lines 35-58 and Column 5, lines 24-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the fiber optic support of Walt et al to the support of Macevicz based on the suggestion of Macevicz to apply known supports based on efficiency and optical properties (Column 14, line 61-Column 15, line 23, especially lines 17-21) and for the expected benefits of exceptional efficiency and optical properties as taught by Walt et al (Column 4, lines 35-58 and Column 5, lines 24-30).

13. Claims 15-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. (U.S. Patent No. 6,027,889, filed 28 May 1997) in view of Ullman et al (U.S. Patent No. 5,185,243, issued 9 February 1993), Collins (U.S. Patent No. 5,750,338, issued 12 May 1998). and Walt et al. (U.S. Patent No. 6,023,540, filed 14 may 1997).

Regarding Claim 29, Barany et al. teach a method of detecting a target nucleic acid sequence comprising: hybridizing a first primer to a first portion of a target sequence wherein said first primer further comprises an adapter sequence; hybridizing a second primer to a second portion of said target sequence; ligating said first and second primers to form a modified primer; contacting said adapter sequence of said modified primer with an array comprising: a substrate with a surface comprising discrete sites comprising at least a first sub-population comprising a first capture probe, such that said first capture probe and said modified first target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified first target nucleic acid sequence (Column 26, line 37-Column 27, line 19 and Claim 13). The extra method steps of Barany et al. are encompassed by the open claim language "comprising" of the instant claims.

Barany et al. do not teach the method wherein the primers are not adjacent. However, Ullman et al teach a similar method comprising: wherein the first and second target regions are not adjacent; extending one of the primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Barany et al by designing primers that hybridize to non-adjacent target positions as taught by Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Barany et al. do not teach the method wherein the array further comprises a population of microspheres comprising the at least first sub-population wherein said microspheres are

distributed on said surface. However, Walt et al. teach a similar method for detecting a target nucleic acid sequence comprising: contacting said first target nucleic acid sequence with an array comprising: a substrate with a patterned surface comprising discrete sites; and a population of microspheres comprising at least a first sub-population comprising a first capture probe such that said first capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said first target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Barany, Walt and Ullman do not teach the target is immobilized on a solid phase surface during hybridization between the first primer and target. However, target immobilization during a first hybridization step was well known in the art at the time the claimed invention was made as taught by Collins (e.g. Fig.6). Collins et al teach a similar method of target detection comprising a first step of hybridizing a first primer and a target, wherein the target is immobilized whereby the target immobilization facilitates removal of non-specific material from the sample and concentrates the target for detection and greater purification of detectable product (Column 5, lines 19-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the target immobilization of Collins et al to the target detection of Barany, Walt and Ullman for the

expected benefit removal of non-specific material from the sample, concentration the target for detection and greater purification of detectable product as taught by Collins (Column 5, lines 19-25).

Regarding Claim 15, Barany et al. teach the method further comprising detecting a second target sequence (i.e. array) thereby comprising hybridizing third and forth primers to first and second portions of the second target; contacting with said array and detecting the presence of said second target (Fig. 9).

Regarding Claim 16, Barany et al. teach the method wherein the modified primer is amplified (Column 27, lines 1-2).

Regarding Claim 17, Barany et al. teach the method wherein said the detecting is done by hybridizing a labeled probe to the ligated primers (Column 33, lines 16-39).

Regarding Claim 18, Barany et al. teach the substrate is an array (Column 27, lines 10-15) but they do not teach the array is a fiber optic bundle. However, Walt et al. teach the similar method wherein the substrate is a fiber optic bundle (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on a fiber optic bindle substrate for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 19, Barany et al. teach said substrate comprises discrete sites (Column 27, lines 10-15) but they do not teach said discrete sites comprise wells. However, Walt et al. teach the similar method wherein said discrete sites comprise wells (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the discrete sites on the substrate of Barany et al. to provide microspheres distributed on a substrate at the discrete sites and wherein each discrete site comprises a well for the expected benefit of individual identification of thousands of captured

target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 20, Barany et al teach the method wherein the detecting is done by labeling amplification products (Column 27, liens 2-19).

Regarding Claim 21, Barany et al teach the method wherein one of the primers is allele specific (Column 25, lines 1-25).

Regarding Claim 22, Barany et al. teach a method of detecting at least sixteen target nucleic acids (i.e. an array, Fig. 9) sequence comprising: hybridizing a first primer to a first portion of a target sequence wherein said first primer further comprises an adapter sequence; hybridizing a second primer to a second portion of said target sequence;ligating said first and second primers to form a modified primer; contacting said adapter sequence of said modified primer with an array comprising: a substrate with a surface comprising discrete sites comprising at least a first sub-population comprising a first capture probe, such that said first capture probe and said modified first target nucleic acid sequence form a hybridization complex; and detecting the presence of said modified first target nucleic acid sequence (Fig. 15, Column 26, line 37-Column 27, line 19 and Claim 13). The extra method steps of Barany et al. are encompassed by the open claim language "comprising" of the instant claims.

Barany et al. do not teach the method wherein the primers are extended toward each other. However, Ullman et al teach a similar method comprising: extending one primer toward the other and ligating said first and second primer to form a modified primer and capturing the modified primer (Column 4, line 45-Column 6, line 5; and Column 9, line 59-Column 10, line 18) wherein the extension of non-adjacent primers eliminates the need to identify the diagnostic sequence thereby facilitating diagnostic detection and increasing the specificity and sensitivity of diagnostic detection (Column 4, lines 3-12). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the primers of Barany et al by designing primers that hybridize to non-adjacent target positions as taught by

Ullman et al for the expected benefit of eliminating the need to identify the diagnostic sequence thereby facilitating diagnostic detection and further increasing the specificity and sensitivity of diagnostic detection as taught by Ullman et al (Column 4, lines 3-12).

Barany et al. do not teach the method wherein the array further comprises a population of microspheres comprising the at least first sub-population wherein said microspheres are distributed on said surface. However, Walt et al. teach a similar method for detecting a target nucleic acid sequence comprising: contacting said first target nucleic acid sequence with an array comprising: a substrate with a patterned surface comprising discrete sites; and a population of microspheres comprising at least a first sub-population comprising a first capture probe such that said first capture probe and said first target nucleic acid sequence form a hybridization complex, wherein said microspheres are distributed on said surface (Column 4, lines 4-14); and detecting the presence of said first target nucleic acid sequence (Column 10, lines 4-41) wherein microspheres comprising different capture probes are mixed but individually detected and identified allowing for individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use (Column 3, lines 17-30). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on the array at discrete site and wherein the microspheres comprise the capture probes for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Barany, Walt and Ullman do not teach the target is immobilized on a solid phase surface during hybridization between the first primer and target. However, target immobilization during a first hybridization step was well known in the art at the time the claimed invention was made as taught by Collins (e.g. Fig.6). Collins et al teach a similar method of target detection comprising a first step of hybridizing a first primer and a target,

wherein the target is immobilized whereby the target immobilization facilitates removal of non-specific material from the sample and concentrates the target for detection and greater purification of detectable product (Column 5, lines 19-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the target immobilization of Collins et al to the target detection of Barany, Walt and Ullman for the expected benefit removal of non-specific material from the sample, concentration the target for detection and greater purification of detectable product as taught by Collins (Column 5, lines 19-25).

Regarding Claim 23, Barany et al. teach the method wherein the modified primer is amplified (Column 27, lines 1-2).

Regarding Claim 24, Barany et al. teach the method wherein said the detecting is done by hybridizing a labeled probe to the ligated primers (Column 33, lines 16-39).

Regarding Claim 25, Barany et al. teach the substrate is an array (Column 27, lines 10-15) but they do not teach the array is a fiber optic bundle. However, Walt et al. teach the similar method wherein the substrate is a fiber optic bundle (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Barany et al. to further comprise microspheres wherein the microsphere are distributed on a fiber optic bindle substrate for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 26, Barany et al. teach said substrate comprises discrete sites (Column 27, lines 10-15) but they do not teach said discrete sites comprise wells. However, Walt et al. teach the similar method wherein said discrete sites comprise wells (Column 4, lines 4-14). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the discrete sites on the substrate of Barany et al. to provide microspheres distributed on a substrate at the discrete sites and wherein each discrete site

comprises a well for the expected benefit of individual identification of thousands of captured target sequences using an apparatus which is easy to manufacture and use as taught by Walt et al. (Column 3, lines 17-30).

Regarding Claim 27, Barany et al teach the method wherein the detecting is done by labeling amplification products (Column 27, liens 2-19).

Regarding Claim 28, Barany et al teach the method wherein one of the primers is allele specific (Column 25, lines 1-25).

***Double Patenting***

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 15-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 and 27-32 of U.S. Patent No. 6,355,431. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to very similar methods for detecting target sequences and differ only in the arrangement of limitations within the claims sets. For example, independent Claims 22 and 29 of the instant invention recite primer extension and

ligation steps. In slight contrast, various dependent claims (e.g. 5-6, 12) define the method as comprising primer extension and/or ligation. As such, the instant claims are an obvious variation of the patent claims.

16. Claims 15-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-31, 42-44, 46, 48 and 50-52 of copending Application No. 09/425,633. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to similar methods of detecting a target and differ only in the '633 claims being drawn to nucleotide target while the instant claims are drawn to a nucleic acid sequence target. However, both sets of claims contain very similar method steps concluding with target detection via detection of ligated product. The '633 nucleotide target is considered a species of the instantly claimed nucleic acid sequence target because the instantly claimed sequence comprise target nucleotides.

The courts have stated that a genus is obvious in view of the teaching of a species see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989).

For all the reasons stated above, the instantly claimed methods are obvious in view of the '633 methods.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

**Conclusion**

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
May 11, 2004